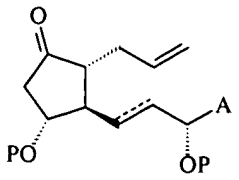
Claims

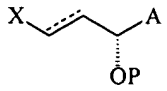
1. A process for the preparation of a compound of formula (VIII):



(VIII)

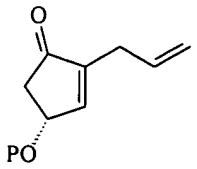
wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond;

comprising converting a compound of formula (IX):



(IX)

wherein A, P and ----- are as defined above and X is a leaving group, to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (X):



(X)

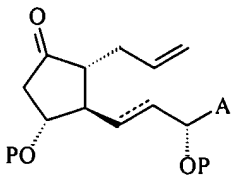
wherein P is as defined above.

2. The process according to claim 1, wherein P is a tetrahydropyranyl (THP) protecting group.

3. The process according to claim 1 or claim 2, wherein X is iodine.

4. The process according to claim 1, wherein A is $(CH_2)_2Ph$, ----- represents a double bond, P is THP and X is I.

5. A compound of formula (VIII):



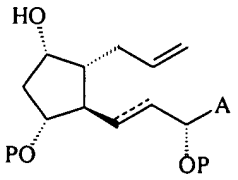
(VIII)

;

wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond.

6. The compound according to claim 5, wherein A is $(CH_2)_2Ph$, ----- represents a double bond and P is THP.

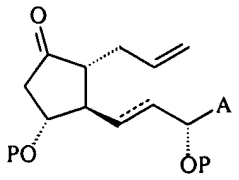
7. A process for the preparation of a compound of formula (VIIa):



(VIIa)

wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group and ----- represents a double bond or a single bond;

comprising selectively reducing a compound of formula (VIII):



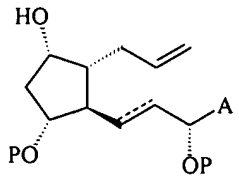
(VIII)

wherein A, P and ----- are as defined above.

8. The process according to claim 7, wherein P is a tetrahydropyranyl (THP) protecting group.

9. The process according to claim 7, wherein A is $(CH_2)_2Ph$, ----- represents a double bond and P is THP.

10. A compound of formula (VIIa):



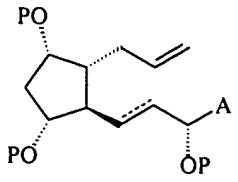
(VIIa)

;

wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond.

11. The compound according to claim 10, wherein A is $(CH_2)_2Ph$, ----- represents a double bond and P is THP.

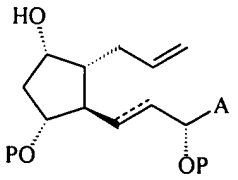
12. A process for the preparation of a compound of formula (VIIb):



(VIIb)

wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group and ----- represents a double bond or a single bond;

comprising protecting a compound of formula (VIIa):



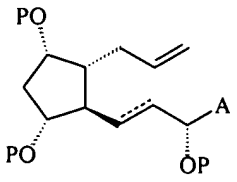
(VIIa)

wherein A, P and ----- are as defined above, with a hydroxyl protecting group.

13. The process according to claim 12, wherein P is a tetrahydropyranyl (THP) protecting group.

14. The process according to claim 12, wherein A is $(CH_2)_2Ph$, ----- represents a double bond and P is THP.

15. A compound of formula (VIIb):



(VIIb)

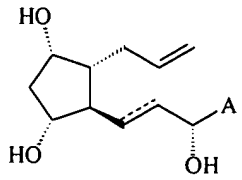
;

wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three

substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond.

16. The compound according to claim 15, wherein A is $(CH_2)_2Ph$, ----- represents a double bond and P is THP.

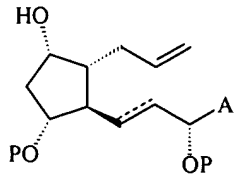
17. A process for the preparation of a compound of formula (VIIc):



(VIIc)

wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3 and ----- represents a double bond or a single bond;

comprising deprotecting a compound of formula (VIIa):



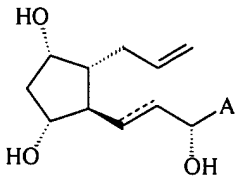
(VIIa)

wherein A and ----- are as defined above and P is a protecting group.

18. The process according to claim 17, wherein P is a tetrahydropyranyl (THP) protecting group.

19. The process according to claim 17 or claim 18, wherein A is $(CH_2)_2Ph$ and ----- represents a double bond.

20. A compound of formula (VIIc):



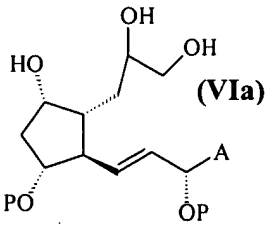
(VIIc)

;

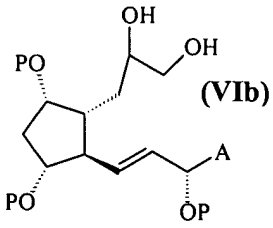
wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond.

21. The compound according to claim 20, wherein A is $(CH_2)_2Ph$ and ----- represents a double bond.

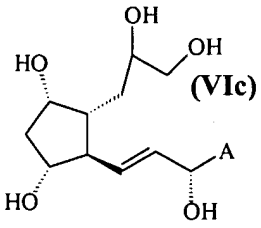
22. A process for the preparation of a compound of formula (VIa), (VIb), (VIc), (Va), (Vb) or (Vc):



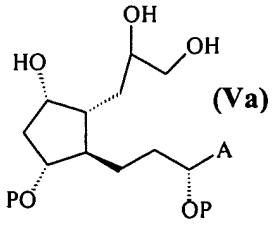
(VIa)



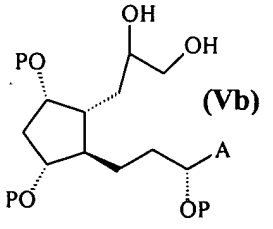
(VIb)



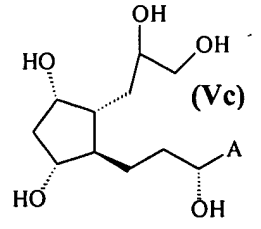
(VIc)



(Va)

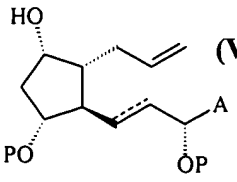


(Vb)

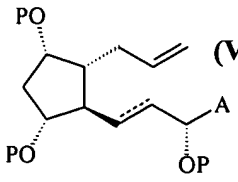


(Vc)

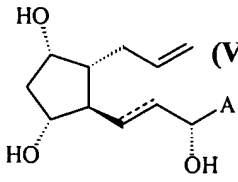
wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and P is a hydroxyl protecting group; comprising dihydroxylating a compound of formula (VIIa), a compound of formula (VIIb) or a compound of formula (VIIc):



(VIIa)



(VIIb)



(VIIc)

wherein A and P are as defined above and ----- is a double or single bond.

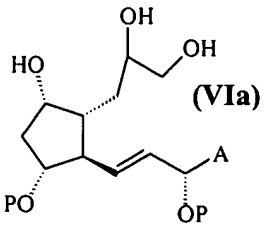
23. The process according to claim 22, wherein P is a tetrahydropyranyl (THP) protecting group.

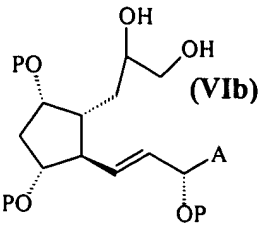
24. The process according to claim 22, wherein A is $(CH_2)_2Ph$, P is THP, ----- represents a double bond, and compound (VIIa) reacts to give compound (VIa).

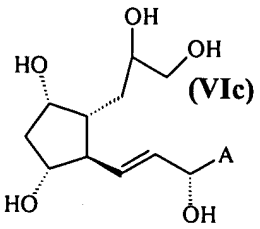
25. The process according to claim 22, wherein A is $(CH_2)_2Ph$, P is THP, ----- represents a double bond, and compound (VIIb) reacts to give compound (VIb).

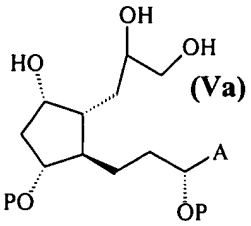
26. The process according to claim 22, wherein A is $(CH_2)_2Ph$, ----- represents a double bond, and compound (VIIc) reacts to give compound (VIc).

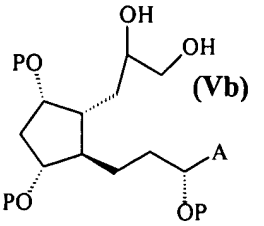
27. A compound of formula (VIa), (VIb) (VIc), (Va), (Vb) or (Vc):

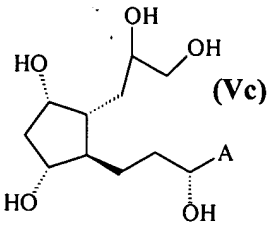








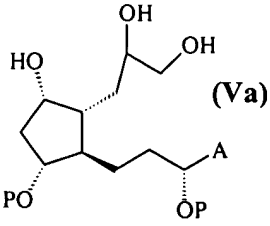


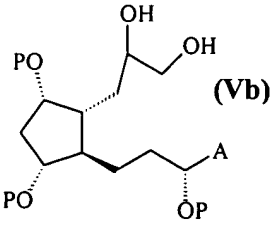


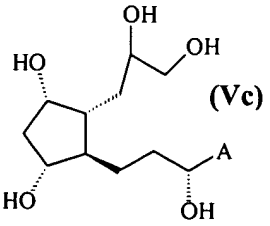
wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group; and ----- represents a double bond or a single bond.

28. The compound according to claim 27, wherein A is $(CH_2)_2Ph$ and P is THP.

29. A process for the preparation of a compound of formula (Va), (Vb) or (Vc):

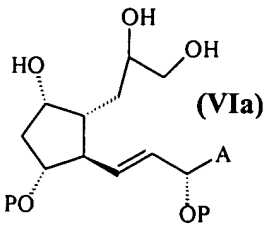


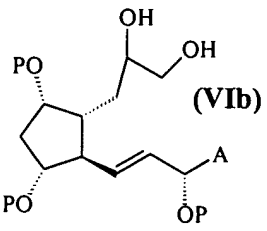


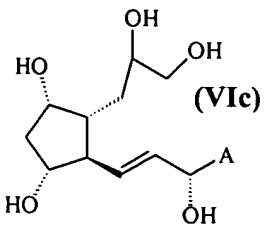


wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which

is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and P is a hydroxyl protecting group; comprising reducing a double bond of a compound of formula (VIa), a compound of formula (VIb) or a compound of formula (VIc):







wherein A and P are as defined above.

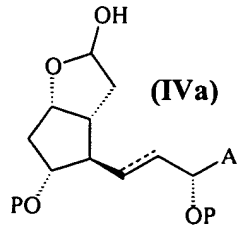
30. The process according to claim 29, wherein P is a tetrahydropyranyl (THP) protecting group.

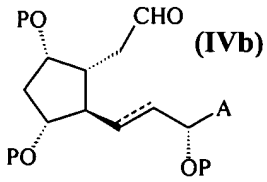
31. The process according to claim 29, wherein A is $(CH_2)_2Ph$, P is THP and compound (VIa) reacts to give compound (Va).

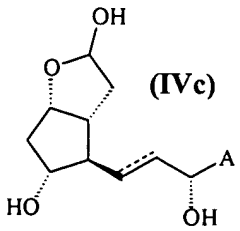
32. The process according to claim 29, wherein A is $(CH_2)_2Ph$, P is THP and compound (VIb) reacts to give compound (Vb).

33. The process according to claim 29, wherein A is $(CH_2)_2Ph$ and compound (VIc) reacts to give compound (Vc).

34. A process for the preparation of a compound of formula (IVa), (IVb) or (IVc):



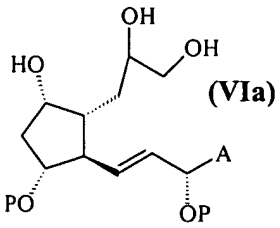


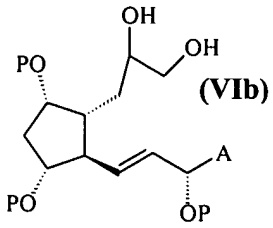


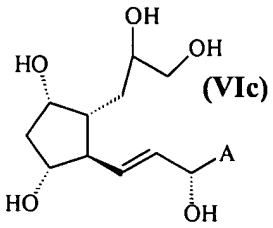
wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three

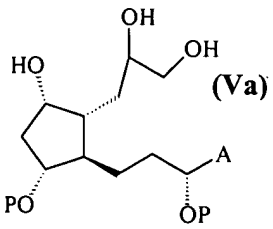
substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; P is a hydroxyl protecting group and ----- represents a double bond or a single bond;

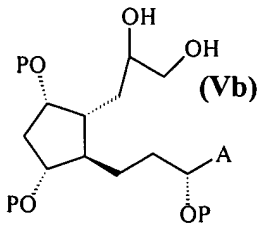
comprising performing a diol cleavage reaction on a compound of formula (VIa), (Va), (VIb), (Vb), (VIc) or (Vc):

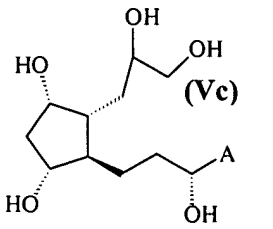












wherein A and P are as defined above.

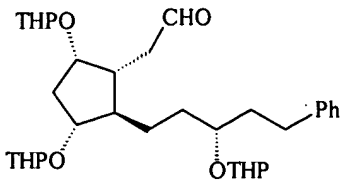
35. The process according to claim 34, wherein P is a tetrahydropyranyl (THP) protecting group.

36. The process according to claim 34, wherein A is $(CH_2)_2Ph$, P is THP, ----- represents a single bond, and compound (Va) reacts to give compound (IVa).

37. The process according to claim 34, wherein A is $(CH_2)_2Ph$, P is THP, ----- represents a single bond, and compound (Vb) reacts to give compound (IVb).

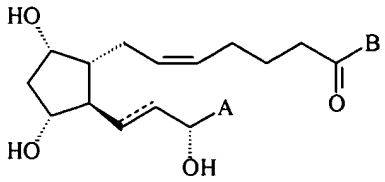
38. The process according to claim 34, wherein A is $(CH_2)_2Ph$, ----- represents a single bond, and compound (Vc) reacts to give compound (IVc).

39. A compound having the formula (14):



(14)

40. A process for the preparation of a prostaglandin compound having the formula (I):

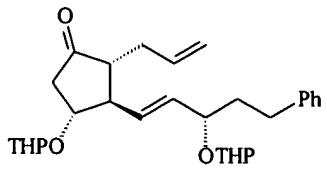


(I)

wherein A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; B is selected from OR" and NHR" wherein R" is C_1-C_6 alkyl groups; and ----- represents a double bond or a single bond; comprising a process according to any one of claims 1, 2, 4, 7-9, 12-14, 17, 18, 22-26 and 29-38.

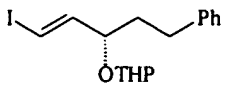
41. A process for synthesising Latanoprost comprising the steps of:

a) preparing a compound of formula (3):



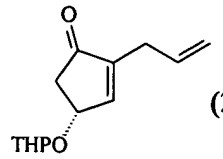
(3)

said preparing comprising converting a compound of formula (1):



(1)

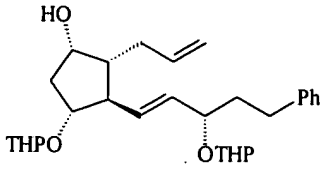
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



(2)

;

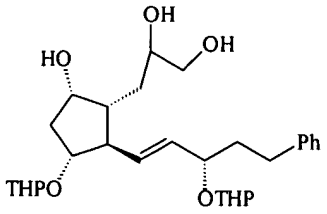
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



(4)

;

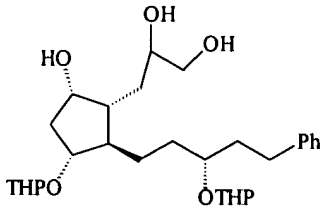
c) dihydroxylating the compound of formula (4) to provide a compound of formula (7):



(7)

;

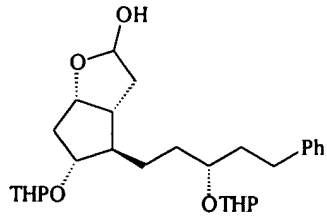
d) reducing the compound of formula (7) to provide a compound of formula (10):



(10)

;

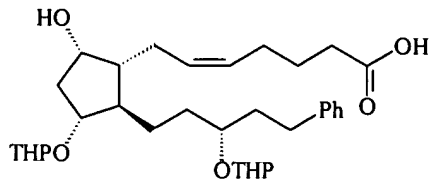
e) performing a diol cleavage reaction on the compound of formula (10) to provide a compound formula (13):



(13)

;

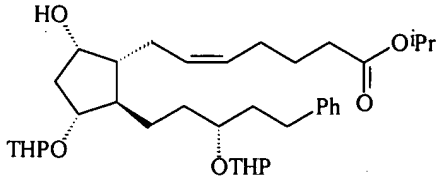
f) performing a Wittig reaction on the compound of formula (13) to provide a compound of formula (16):



(16)

;

g) esterifying the compound of formula (16) to provide a compound of formula (19):

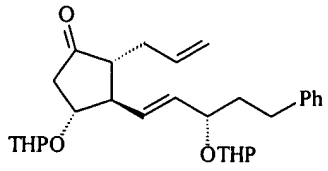


(19); and

h) deprotecting the compound of formula (19) to provide Latanoprost.

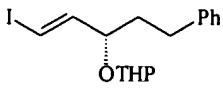
42. A process for synthesising Latanoprost comprising the steps of:

a) preparing a compound of formula (3):



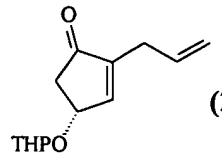
(3)

said preparing comprising converting a compound of formula (1):



(1)

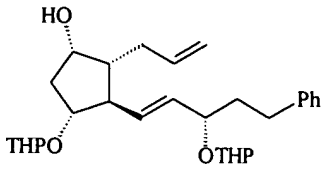
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



(2)

;

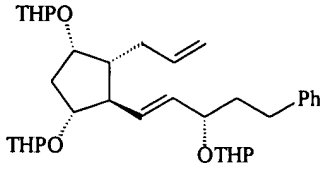
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



(4)

;

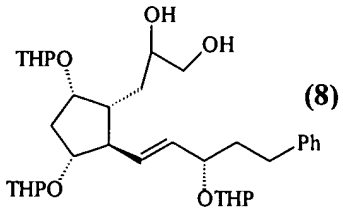
c) protecting the compound of formula (4) to provide a compound of formula (5):



(5)

;

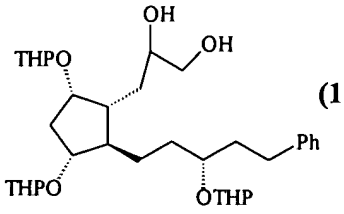
d) dihydroxylating the compound of formula (5) to provide a compound of formula (8):



(8)

;

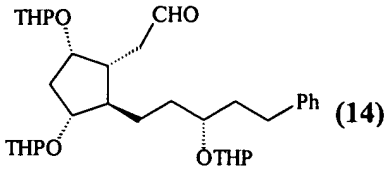
e) reducing the compound of formula (8) to provide a compound of formula (11):



(11)

;

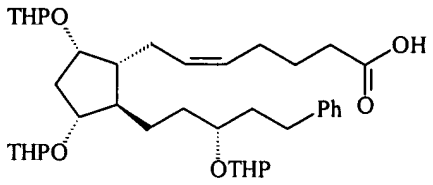
f) performing a diol cleavage reaction on the compound of formula (11) to provide a compound of formula (14):



(14)

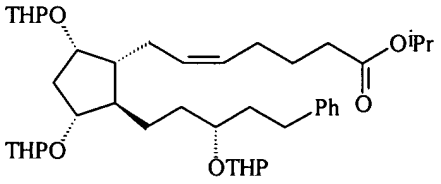
;

g) performing a Witting reaction on the compound of formula (14) to provide a compound of formula (17):



(17);

h) esterifying the compound of formula (17) to provide a compound of formula (20):

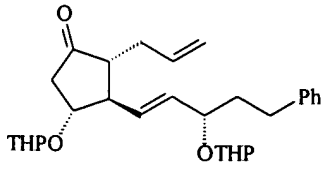


(20); and

i) deprotecting the compound of formula (20) to provide Latanoprost.

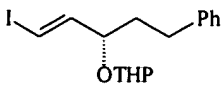
43. A process for synthesising Latanoprost comprising the steps of:

a) preparing a compound of formula (3):



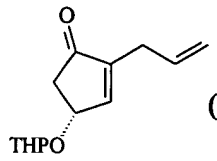
(3)

said preparing comprising converting a compound of formula (1):



(1)

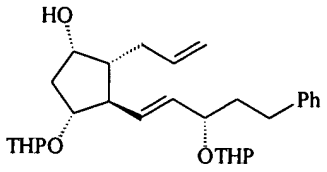
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



(2)

;

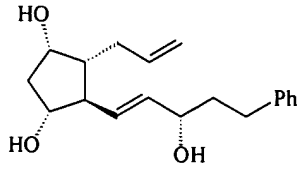
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



(4)

;

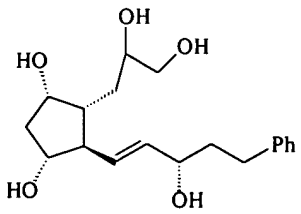
c) deprotecting the compound of formula (4) to provide a compound of formula (6):



(6)

;

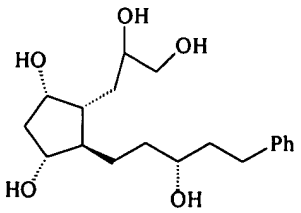
d) dihydroxylating the compound of formula (6) to provide a compound of formula (9):



(9)

;

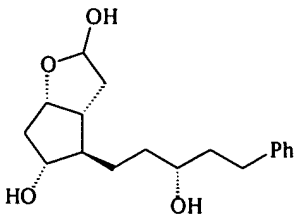
e) reducing the compound of formula (9) to provide a compound of formula (12):



(12)

;

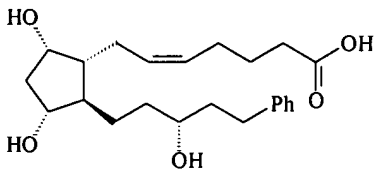
f) performing a diol cleavage reaction on the compound of formula (12) to provide a compound of formula (15):



(15)

;

g) performing a Wittig reaction on the compound of formula (15) to provide a compound of formula (18):



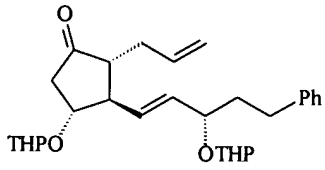
(18)

; and

h) esterifying the compound of formula (18) to provide Latanoprost.

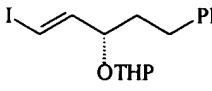
44. A process for synthesising Bimatoprost comprising the steps of:

a) preparing a compound of formula (3):



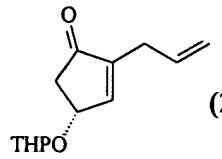
(3)

said preparing comprising converting a compound of formula (1):



(1)

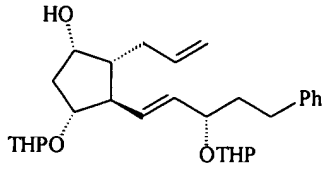
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



(2)

;

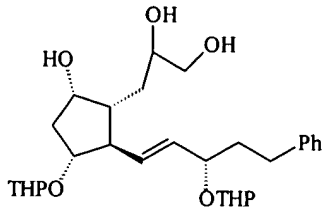
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



(4)

;

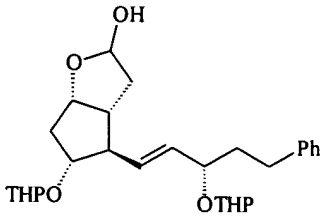
c) dihydroxylating the compound of formula (4) to provide a compound of formula (7):



(7)

;

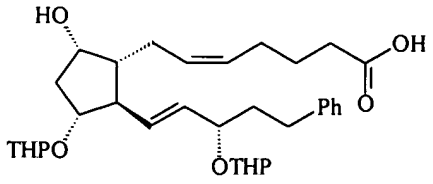
d) performing a diol cleavage reaction on the compound of formula (7) to provide a compound of formula (23):



(23)

;

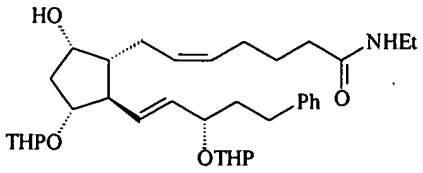
e) performing a Wittig reaction on the compound of formula (23) to provide a compound of formula (26):



(26)

;

f) amidating the compound of formula (26) to provide a compound of formula (29):



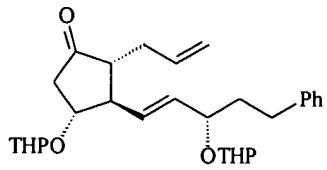
(29)

; and

g) deprotecting the compound of formula (29) to provide Bimatoprost.

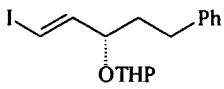
45. A process for synthesising Bimatoprost comprising the steps of:

a) preparing a compound of formula (3):



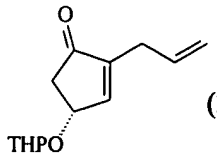
(3)

said preparing comprising converting a compound of formula (1):



(1)

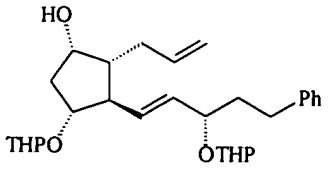
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



(2)

;

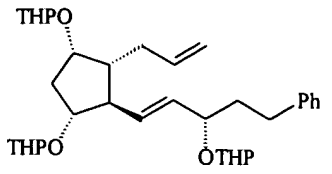
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



(4)

;

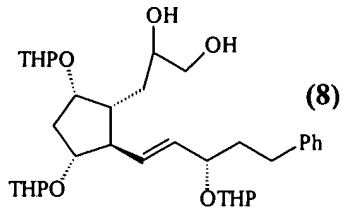
c) protecting the compound of formula (4) to provide a compound of formula (5):



(5)

;

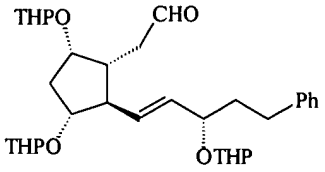
d) dihydroxylating the compound of formula (5) to provide a compound of formula (8):



(8)

;

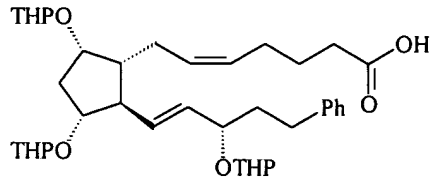
e) performing a diol cleavage reaction on the compound of formula (8) to provide a compound of formula (24):



(24)

;

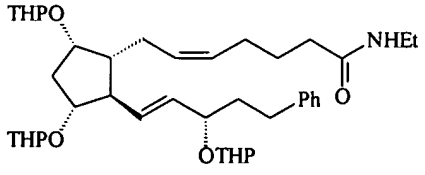
f) performing a Wittig reaction on the compound of formula (24) to provide a compound of formula (27):



(27)

;

g) amidating the compound of formula (27) to provide a compound of formula (30):



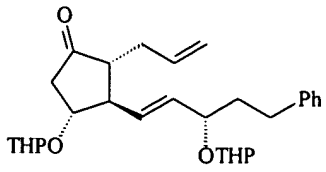
(30)

; and

h) deprotecting the compound of formula (30) to provide Bimatoprost.

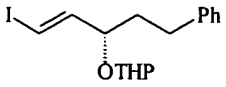
46. A process for synthesising Bimatoprost comprising the steps of:

a) preparing a compound of formula (3):



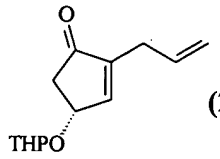
(3)

said preparing comprising converting a compound of formula (1):



(1)

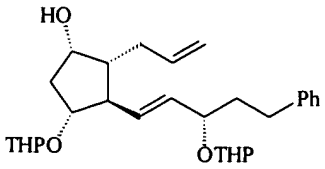
to a cuprate reagent and performing a 1,4 addition reaction between the cuprate reagent and a compound of formula (2):



(2)

;

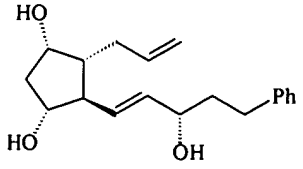
b) selectively reducing the compound of formula (3) to provide a compound of formula (4):



(4)

;

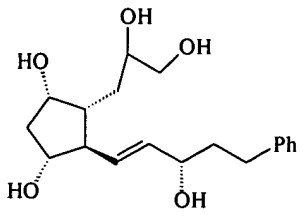
c) deprotecting the compound of formula (4) to provide a compound of formula (6):



(6)

;

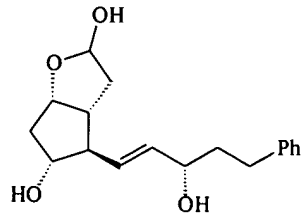
d) dihydroxylating the compound of formula (6) to provide a compound of formula (9):



(9)

;

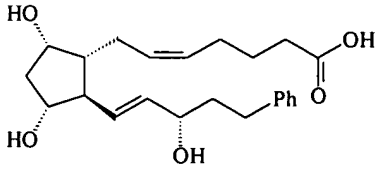
e) performing a diol cleavage on the compound of formula (9) to provide a compound of formula (25):



(25)

;

f) performing a Wittig reaction on the compound of formula (25) to provide a compound of formula (28):



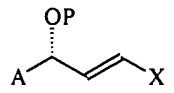
(28)

; and

g) amidating the compound of formula (28) to provide Bimatoprost.

47. A process for synthesising Travoprost comprising a process according to any one of claims 1, 2, 7-8, 12-13, 17-18, 22-23, 29-30 and 34-35.

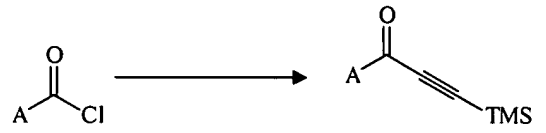
48. A process for synthesising a compound of formula (IX):



(IX)

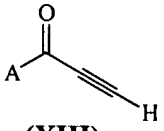
comprising the steps of:

a) reacting an acid chloride of formula (XV) with a bis(trialkylsilylacetylene) to form an acetylene of formula (XIV):



(XV) **(XIV)** ;

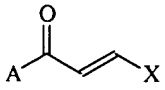
b) reacting the acetylene of formula (XIV) with a reducing agent to form an acetylene of formula (XIII):



(XIII)

;

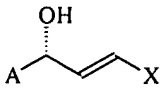
c) hydrohalogenating the acetylene of formula (XIII) to form a vinyl halide comprising a prochiral ketone according to formula (XII);



(XII)

;

d) stereoselectively reducing the prochiral ketone in the vinyl halide of formula (XII) to form a vinyl halide comprising a hydroxy group according to formula (XI); and



(XI) ; and

e) protecting the hydroxy group in the vinyl halide of formula (XI) to provide the compound of formula (IX);

wherein X is a halogen; P is a hydroxyl protecting group; and A is selected from the group consisting of C_1-C_6 alkyl groups; C_7-C_{16} aralkyl groups wherein an aryl portion thereof is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3; and $(CH_2)_nOR'$ wherein n is an integer from 1 to 3 and R' represents a C_6-C_{10} aryl group which is unsubstituted or substituted with one to three substituents selected from the group consisting of C_1-C_6 alkyl groups, halo and CF_3.